a variety of structural defects including short palpebral fissures, a long philtrum with a thin smooth upper lip, multiple joint anomalies and cardiac defects. It has become clear that the fetal alcohol syndrome as it was initially delineated represents only a part of a more extensive problem. There are, for example, a large number of children born to women who drink either heavily or moderately during pregnancy who have features compatible with the prenatal effects of alcohol but who do not have the full-blown fetal alcohol syndrome. In a recent study from the University of Göteborg in Sweden, it was estimated that for every full-blown case of the syndrome, there is at least one child born with features compatible with the prenatal effects of alcohol who does not have the full-blown syndrome. In that prospective study, Olegard and co-workers determined that 33 percent of the offspring of alcoholic women who continued to drink heavily during pregnancy had the fetal alcohol syndrome and an additional 33 percent had features consistent with the prenatal effect of alcohol; only 33 percent of the offspring were normal. With respect to moderate alcohol consumption, Hanson and colleagues have estimated that 11 percent of the offspring of women who drink between one and two ounces of absolute alcohol a day during the first trimester of their pregnancy have features consistent with the prenatal effects of alcohol. For lesser amounts of alcohol, particularly "binge drinking" during pregnancy, no data are available.

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Gastrointestinal Disease

SEVERAL new viral, bacterial and parasitic agents that cause gastrointestinal disease have been identified in recent years. Studies from different parts of the world have shown that up to 75 percent of acute diarrheal disease is nonbacterial. Rotavirus is the most important viral agent causing sporadic and epidemic outbreaks of diarrheal disease in those 2 years and younger. It occurs typically in winter, causing fever and diarrhea; vomiting is less prominent. Symptoms may persist for up to eight days. Parvovirus agents, including the Norwalk agent, have been found to cause diarrhea, fever and vomiting that last one to two days in children and adults. Viral gastroenteritis is treated with supportive care.

Campylobacter fetus, formerly classified as *Vibrio fetus,* has been recognized as a common cause of diarrhea in children and adults. In a recent Canadian study, *Campylobacter fetus* subspecies *jejuni* was second only to *Salmonella* as a bacterial cause of diarrhea in children. It was not recovered from stool specimens of children without symptoms. The illness was characterized by fever, abdominal pain, which may be severe, and diarrhea, which may recur. Spread throughout a household is common and pets are possible sources of this disease. No controlled studies of treatment have been reported. Isolates are usually sensitive to erythromycin, aminoglycosides, chloramphenicol and tetracycline but resistance may develop during treatment.

Yersinia enterocolitica causes gastroenteritis in children and adults. Young children often have fever, vomiting and diarrhea and leukocytes may be present in the stool. Older children may present with pseudoappendicitis, fever and abdominal pain; mesenteric lymphadenitis occurs in some cases. Adults with *Y enterocolitica* are also affected with gastroenteritis and, at times, erythema nodosum and arthritis. This infection should be considered in pseudoappendicitis, and serological test and culture are useful in establishing the diagnosis. *Y enterocolitica* has been recovered from a variety of sources including raw milk, water supplies and wild and domestic animals. Transmission can occur from other humans or from pets, and the incubation period is usually four to ten days. The efficacy of antibiotic drugs in treating active disease is unknown as is the effect on the carrier state.

Giardia lamblia, an intestinal flagellate, has been recognized as a cause of diarrhea in travelers in many parts of the world. In the past few years, outbreaks of giardiasis have occurred in the United States resulting from consumption of contaminated water supplies and person-to-person transmission. A water supply not sufficiently chlorinated may contain *Giardia* cysts. Higher chlorine concentrations or additional treatment such as coagulation flocculation, settling or filtration is needed to kill the organisms. Humans and beavers may be natural reservoirs. Persons infected with *G lamblia* may be asymptomatic car-

riers of the cysts or may have chronic diarrhea, abdominal discomfort and weight loss. The average incubation period is nine days. In the acute stage, explosive diarrhea, which is watery and foul, abdominal cramping and flatulence occur, and the diarrhea and abdominal pain may continue intermittently for months. Examination of stool specimens for ova and parasites between episodes may give negative results. Because the trophozoites are found in the upper small intestine, if repeated stool examinations are negative, duodenal intubation and aspiration may be useful in making the diagnosis. Treatment of adults with 100 mg of quinacrine three times a day for seven days give excellent results. Metronidazole therapy with 250 mg three times a day for seven days also is effective. Pediatric treatment and dosage information is provided in the first reference below.

Any outbreak of infectious diarrhea is a public health problem. Professional food handlers, medical personnel and those employed in child care should not be permitted to work while they have acute diarrhea that may be infectious. If specific bacterial infection is recognized, stool specimens should be obtained and found negative for the organism before work is resumed and local health departments should be notified.

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Side Effects of Human Diploid Cell Rabies Vaccine and Human Rabies Immune Globulin

HUMAN DIPLOID CELL RABIES VACCINE (HDCV), licensed for use in the United States since mid-1980, is an inactivated vaccine prepared from rabies virus grown in human diploid cell cultures. This product is much more immunogenic than the duck embryo rabies vaccine (DEV), the use of which declined drastically after licensure of HDCV. The manufacture of DEV ceased production in November 1981. Human rabies immune globulin (HRIG, or RIG), used to provide rapid but temporary protection, consists of antirabies gamma globulin prepared from plasma of immunized human donors.

Preexposure rabies prophylaxis, given to persons at special risk for rabies (such as veterinarians, animal control personnel and certain laboratory workers) consists of three 1-ml intramuscular injections of HDCV, the second given a week after the first and the third two to three weeks after the second. Prophylaxis for persons with a bite, scratch or saliva-to-mucous-membrane contact from a proved or suspected rabid animal consists of one intramuscular injection of HRIG, dosage based on body weight, and five intramuscular injections of HDCV, the first given the same day as HRIG and the other given 3, 7, 14 and 28 days later. Because HDCV has proved to be so highly immunogenic, collection of a serum specimen for rabies antibody testing after preexposure or postexposure prophylaxis is now recommended only for persons who received DEV or who may be immunocompromised.

Serious side effects are less frequent with HDCV than with DEV. No neuroparalytic reactions have been noted following HDCV; in about one in every 25,000 persons vaccinated with DEV transverse myelitis, encephalopathy, or cranial or peripheral neuropathy developed. One instance of Guillain-Barré syndrome (GBS) following HDCV has been reported. Isolated cases of GBS have been reported following administration of many vaccines, and it has been difficult to determine if causal relationships exist in such episodes. Local reactions, such as pain, redness or pruritus, have been reported in about 25 percent of HDCV recipients, while mild systemic reactions, such as fever, headache, nausea, diarrhea, abdominal pain, myalgia and dizziness, have been reported in 20 percent. Local or mild systemic reactions to HDCV usually can be managed with agents like aspirin and do not necessitate stopping prophylaxis. Rarely, allergic reactions ranging from hives to anaphylactic shock have been reported in HDCV recipients. If a severe allergic reaction occurs before completion of a HDCV series, the risk of rabies developing must be balanced against the risk of continuing administration of HDCV. In these situations, consultation may be obtained from state health departments and the Centers for Disease Control. Pregnancy is not a contraindication for HDCV.

Local pain and low-grade fever may occur in HRIG recipients, but more serious reactions have not been reported. Presumably, adverse reactions such as those reported rarely after use of immunoglobulin (IG; formerly called ISG or GG), including angioneurotic edema, nephrotic syndrome and anaphylaxis, could occur after HRIG. To reduce